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GLYCERALDEHYDEPHOSPHATE DEHYDROGENASE AND GLUCOSE-6-PHOSPHATE DEHYDROGENASE ACTIVITIES IN PSORIASIS AND NEURODERMATITIS AND THE EFFECT OF DITHRANOL*

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ABSTRACT

The subcorneal and basal parts of the germinal epithelium were microdissected from freeze-dried sections originating within or just outside guttate psoriatic and neurodermite lesions. The activity of glyceradehydephosphate dehydrogenase (EC 1.2.1.12)† and glucose-6-phosphate dehydrogenase (EC 1.1.1.49)† was measured by application of Lowry's microtechniques. The activities of both enzymes displayed a similar pattern with a significant rise in the uninvolved part of the border region of the psoriatic lesion. The increase was greater within the lesion. In the neurodermite lesion an increase was obtained only within the lesion and the activities found were lower than those encountered in psoriasis. A significant correlation was also found between the two enzymes.

After treatment with dithranol (1,8,9-trihydroxyanthracene)† the activities of the two enzymes in the psoriatic epidermis were depressed in the border region of the blanched non-scaling lesion and within the lesion. The decrease in the activity of glyceraldehydephosphate dehydrogenase was shown to occur only in the basal epidermis. Glucose-6-phosphate dehydrogenase displayed a decreased activity within the treated lesion in both the subcorneal and basal parts of the epidermis. After treatment the correlation between the activities of the two enzymes could no longer be discerned.

Increased metabolic activity together with enhanced epidermal proliferation are found by histochemical methods in the psoriatic lesion (1, 2). In the border region of a guttate plaque this activity is decreased and farther from the lesion it is equal to that of normal skin (1, 3–6). By application of Lowry's microtechniques (7, 8) the psoriatic skin has been further characterized enzymatically. On dissected material taken from the basal part of the germinative epithelium glyceraldehydephosphate dehydrogenase (GAPDH) was measured from different sites near and within a guttate psoriatic lesion (9). Increased activity was found within the lesion and in its border region. In the present investigation this study is extended. GAPDH and glucose-6-phosphate dehydrogenase (G6PDH) were chosen, since both of them have markedly increased activities in psoriatic lesions (9). Treatment of the patients with a dithranol paste was also studied in order to relate the enzymatic activities to regressive changes induced by an antipsoriatic agent. The neurodermite lesion, which is another acanthotic process, was included as a control.

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† Glyceraldehydephosphate dehydrogenase (EC 1.2.1.12. GAPDH), glucose-6-phosphate dehydrogenase (EC 1.1.1.49. G6PDH), dithranol: 1,8,9-trihydroxyanthracene (Cignolin®).

MATERIAL AND METHODS

Twenty patients, 17 to 52 years old, with guttate psoriasis from a few weeks up to 22 years (mean duration 7 years) were investigated together with four patients, 26 to 70 years old, with neurodermatitis of 2 to 6 years duration. They had not been treated for at least one month before the study was undertaken. Except for the skin disease they declared themselves healthy. Punch biopsies were taken from different sites on the forearm. One was taken from the center of a guttate psoriatic or neurodermite lesion, 5–10 mm in diameter; another was punched from its border region, whose edge had been marked (Fig. 1b). In

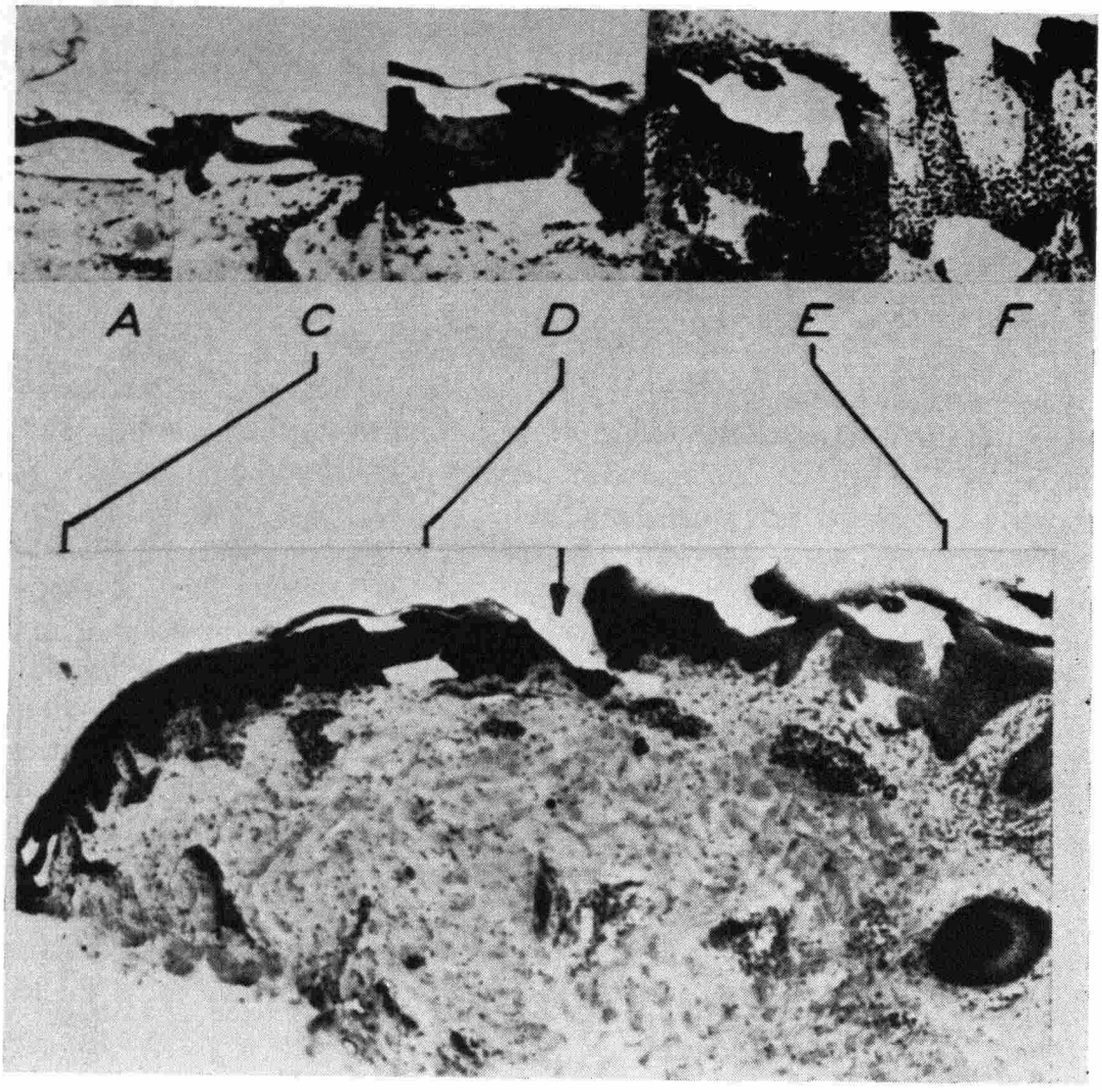

FIG. 1*a*. Sections from a psoriatic patient taken from the following sites: A, non-involved skin; border region of a psoriatic plaque; C, the non-involved part; D, the intermediate part; E, the involved part; F, center of a lesion. The sections have been stained after removal of the microdissected samples. As seen from the epidermal defects, two samples have been taken on each section, the subcorneal one consisting of the granular and upper part of the prickle cell layers, and the basal one consisting of the lower part of the prickle and basal cell layers. × 230. 1*b*. Section from the border region of a plaque illustrating the sites on the section from which the samples C, D and E in Fig. 1*a* have been taken. The arrow indicates the cut made before the biopsy in order to mark the margin of lesion. × 100.

addition, biopsies were collected one and four centimeters from the lesion.

After the biopsies were taken, seven of the psoriatic patients were treated with a dithranol paste (dithranol 0.1, salicylic acid 2, zinc oxide 12, starch 12 and white petrolatum to 100 gram) alternating with 2 per cent salicylic acid in a cream base. On the forearm the dithranol paste was rubbed into both the uninvolved skin and the psoriatic patches. After three weeks the lesions had completely blanched. At this time another set of biopsies was taken from the same area as before.

In most cases the epidermal specimens were dissected both from the subcorneal and the adjacent basal part of the germinal epithelium. In performing these dissections care was taken to obtain samples of the subcorneal and the basal epidermis from the same part of the section, as illustrated by Figure 1. In the biopsy from the border region specimens were taken from the same section both from the unaffected and from the involved part of the epidermis, as well as from the epidermal part in between (sites C, D, E, Fig. 1). The measurements of GAPDH and G6PDH were performed as described in the preceding paper (9). The statistical treatment, mainly analyses of variance, was carried out according to Snedecor (10) and Seeger (11). The coefficients of variation obtained for the assays of GAPDH and G6PDH were 16 and 13 per cent respectively.

RESULTS

Untreated psoriasis and neurodermatitis. The activities of GAPDH and G6PDH obtained from the subcorneal and the basal parts of the germinal epithelium are summarized in Figure 2. For GAPDH a significant difference was shown between psoriasis and neurodermatitis ($P < 0.001$). In psoriasis, as illustrated in

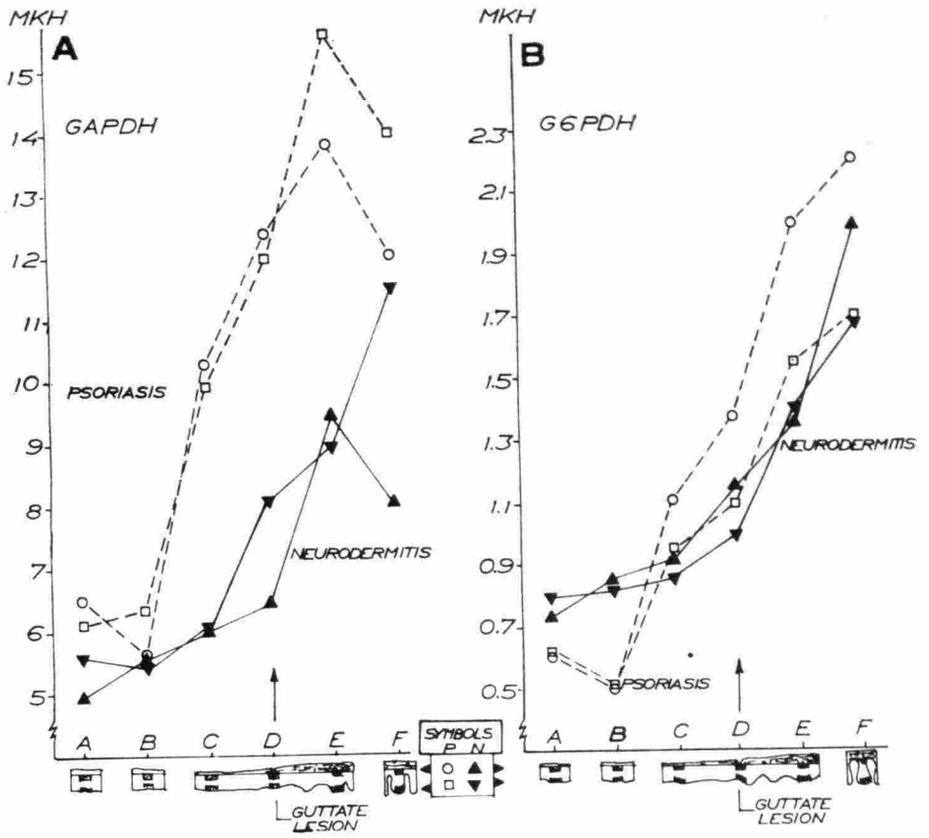

FIG. 2. Activities of (a) glyceraldehydephosphate dehydrogenase (GAPDH) and (b) glucose-6-phosphate dehydrogenase (G6PDH) as related to structural changes. The subcorneal and basal parts of the germinal epithelium have been sampled from the different locations indicated at the bottom of the diagrams. The arrow indicates the boundary between the unaffected skin and the lesion.

Figure 2a, the enzymatic activity increased markedly in the border region of the lesion and the comparison made between the sites B and C was highly significant ($P < 0.001$). In neurodermatitis the corresponding increase was obtained only in the intralesional sites where the activities generally were lower than those in psoriasis. For both of the lesions, on the other hand, the two epidermal layers studied displayed the same enzymatic activity.

The activity of G6PDH increased in the sites near and within the psoriatic lesion, as shown by Figure 2b. Thus, a significant difference was obtained outside the lesion, *i.e.* between the sites B and C ($P < 0.001$). In the subcorneal layers a higher activity also was noted, especially within the psoriatic patch ($P < 0.05$). In neurodermatitis a rise in the enzymatic activity was evident only in the lesion and the activity in the two layers studied showed a similar pattern all through the various sites.

Since GAPDH and G6PDH were assayed from the same biopsy material, a study of their mutual relationship was made. Significant correlations were found between the activities of the two enzymes for the subcorneal and the basal epidermis in both psoriasis and neurodermatitis ($P < 0.01$). An analysis of covariance indicated that the activities of the two enzymes increased similarly in psoriasis and neurodermatitis. When the two epidermal layers were compared, however, it seemed that the rise of G6PDH corresponded to a comparably smaller increase of GAPDH in the subcorneal epithelium when compared to the basal epidermis ($P < 0.05$).

Effects of treatment with dithranol. In seven patients the effect of the treatment with dithranol was studied and the results obtained are summarized in Figure 3. Dithranol was shown to decrease the enzymatic activity of GAPDH mainly in the basal epidermis, since the difference between the layers was significant ($P < 0.001$). Outside the blanched lesion no significant alteration was obtained in the basal germinal epithelium. However, this was probable for the subcorneal epidermis between the sites A and C ($P < 0.05$). On the other hand, the effects of dithranol affected all the sites which had an increased enzymatic activity in the untreated lesion (Fig. 3a).

The effect of dithranol on G6PDH altered the enzymatic activity in both epidermal lay-

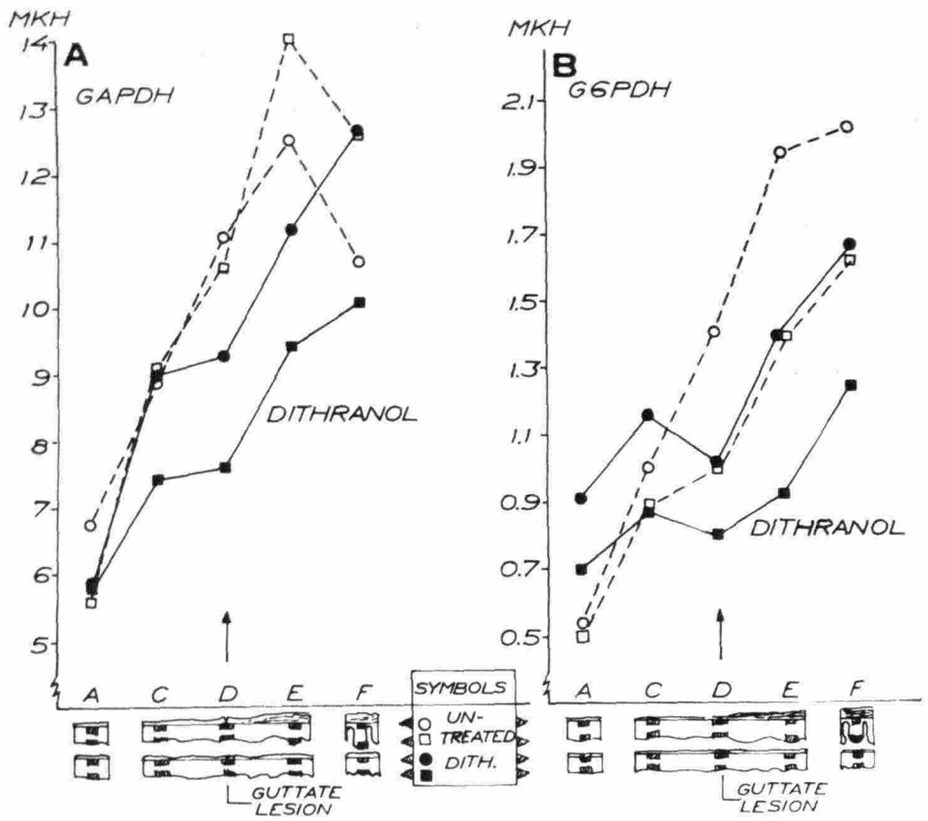

FIG. 3. Activities of (a) glyceraldehydephosphate dehydrogenase and (b) glucose-6-phosphate dehydrogenase as related to structural changes before (hatched lines) and after treatment with dithranol (continuous lines). The convention is the same as in Figure 2.

ers. As shown above, the activity in the subcorneal epidermis was higher when compared to the basal epithelium and this was not changed during the treatment. As visualized in Figure 3b, the activities were leveled in the unaffected part of the border region and an increase was evident only within the blanched lesion. This alteration of the enzymatic pattern, as related to the various sites, was also found to be significant ($P < 0.001$). After treatment with dithranol the correlation between GAPDH and G6PDH was lost. In some patients the decreased activity was mainly limited to one of the enzymes, in others both enzymes were affected.

DISCUSSION

The distribution of the activities of GAPDH and G6PDH in the border region of the psoriatic lesion shows that the enzymatic activity is altered in the area free of erythema and scaling. The reason for this may be that the epidermal cells near the plaque are influenced by the psoriatic process leading to an expansion of the lesion. The margin of the psoriatic plaque is clearly outlined (Fig. 1b). As shown by Van Scott (12) the proliferation of the epidermal cells is mainly perpendicular to the surface which is consistent with the observed pattern in the border region, where the enzymatic activities change rapidly. This indicates that the increased activities of GAPDH and G6PDH within the uninvolved part of the border region is caused by a factor preceding morphological alteration rather than by cells migrating from the psoriatic lesion.

Within the neurodermite lesion the distribution of the two enzymatic activities share some common features with psoriasis, but a difference was obtained in the border region of the lesions. The unchanged enzymatic activities outside the neurodermite lesion clearly differentiate this from the guttate psoriatic lesion with its active border. The guttate psoriatic lesion can be interpreted as being in a state of incipient propagation, which in fact is often seen during the natural course of the disease. The neurodermite lesion is, on the other hand, mostly stationary. It is important, however, that the relationship found between the measured enzymes varies in the same way in both diseases. The correlation found between the enzymatic activities implies that the regulation of the two enzymes takes place through a common control system. The disease only seems to affect the level to which the enzy-

matic activities will be brought. Therefore, the measured activities indicate the metabolic requirements met by the glycolysis and the pentose shunt and they do not disclose the etiology behind the disease.

During the treatment with dithranol a change in the activities of both enzymes is encountered. This is shown in the border region of the psoriatic lesion (Fig. 3). Within the blanched lesion, on the other hand, the enzymatic activities are still comparatively high. The correlation between GAPDH and G6PDH observed in the untreated epidermis is abolished during treatment. The results imply that dithranol may influence the synthesis of the enzymes or the regulation of the enzymatic activities. An inhibitory effect of dithranol on DNA synthesis has been observed in mammalian skin (13) and petite mutants have been induced by dithranol on yeast (14). In the psoriatic lesion the activity of other epidermal enzymes, *e.g.* hexokinase (EC 2.7.1.1.) and phosphofructokinase (EC 2.7.1.11.), was decreased after treatment with dithranol (15).

The blanched lesions obtained by the treatment with dithranol still show increased enzymatic activities, in spite of a good clinical result. This may account for some of the relapses which appear after a treatment period.

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